REMARKS

Claims 1-29, 31, and 34-81 were pending in the application. Claims 1-29 and 36-81 were withdrawn from consideration as directed to non-elected inventions. Claim 31 has been amended to remove dependency on a withdrawn claim. Claim 34 has been amended so it is not a duplicate of claim 31. Claim 36 has been amended so that it depends on claim 31 instead of a withdrawn claim. Claims 82-89 have been added. Support for claims 82-89 can be found throughout the specification and for example at pages 10-20 of the specification as filed. Upon entry of this amendment claims 31, 34, 35 and 82-89 will be pending.

No new matter has been added.

Objections

Claims 31, 34, and 35 stand objected to under 37 C.F.R § 1.75(c) as allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 31 has been amended to remove the dependency upon a non-elected claim, thereby rendering the objection moot. Additionally, claims 31 and 34 have been amended so that the claims no longer have scope that is so similar that they duplicate one another.

In view of the foregoing, Applicants respectfully request that the objections be withdrawn.

Rejection under 35 U.S.C. § 101

Claims 31, 34, and 35 stand rejected under 35 U.S.C. § 101 because the claimed invention is allegedly drawn to an invention with no apparent or disclosed specific and substantial credible utility. The Office also alleges that

> the instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose a specific biological role for this protein or its significance to a particular disease, disorder of physiological process which one would wish to manipulate for a desired clinical effect

(Office Action, pages 3-4). Applicants respectfully disagree.

Utility Examination Guidelines

The Utility Examination Guidelines require that a claimed invention have a specific, substantial and credible asserted utility, or, alternatively a well-established utility. As Applicants have asserted utilities that are specific, substantial and credible and well-established, the Utility Requirement has been satisfied. Applicants therefore respectfully request the withdrawal of the rejection under 35 U.S.C. § 101.

The Utility Examination Guidelines require a claimed invention to have a utility that is specific to the subject matter claimed (a "specific utility"). The present application recites at, for example, pages 43-47 of the specification that the claimed invention can be used, *inter alia*, to identify ligands and/or protein binding partners. Additionally, the polypeptides of the present invention can be used to generate antibodies useful to localize the protein *in vivo* or *in vitro*. For example, the specification teaches that Con-218 is expressed in the brain, testis, and hypothalamus, (see, *inter alia*, pages 85-87). Thus, antibodies generated against the polypeptides of the present invention can be used to identify the origin of cells and/or tissues as being from the brain, hypothalamus, and/or testis. Being able to identify specific tissue types in the brain can also be used to identify defects and abnormalities in the brain by the absence or presence of staining of Con-218. Such antibodies also allow the skilled-artisan to follow the development of the fetal brain to determine when areas of the brain develop based upon the antibody staining of Con-218. Thus, there is no question that Applicants have asserted at least one specific utility and, in fact, have provided numerous specific utilities for the polypeptides of the present invention.

It appears that the Office is under the impression that ***absolute*** certainty is required for a polypeptide to have a specific utility. The Office states, "There is little doubt that, after complete characterization, this protein will probably be found to have a patentable utility. This further characterization, however, is part of the act of invention

and, until it has been undertaken, Applicants' claimed invention is incomplete." (Office Action, page 4).

The standard applicable in this case is not, however, proof to certainty, but rather proof to reasonable probability. As the Supreme Court stated applicant need only prove a "substantial likelihood" of utility; certainty is not required. *Brenner v. Manson*, 383 U.S. at 532. Although there may be numerous inventions that may arise from the present application this standard does not justify the Office's stance that the present invention lacks a specific utility. Thus, Applicants have complied with the specific utility requirement.

The Claimed Invention Has A Substantial Utility

The Utility Examination Guidelines also require a claimed invention to have a utility that defines a real-world use (a "substantial utility"). Applicants teach, as described above, that the claimed invention can be used to make antibodies, identify ligands and other binding partners, such as other proteins that interact with the polypeptide (i.e. a G protein). Thus, it is clear that the claimed invention has real-world uses. All the uses described in the present application are real-world uses and, again, stand in stark contrast to the "throw away" uses (e.g., landfill component or snake food) set forth in the utility guidelines. Thus, there is no question that Applicants have asserted at least one substantial utility and, in fact, have provided numerous substantial utilities. Accordingly, Applicants have complied with the substantial utility requirement.

The Claimed Invention Has A Credible Utility

In addition to a specific and substantial utility the Utility Examination Guidelines require that such utility be credible (a "credible utility"). That is, whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided. Clearly, the numerous specific and substantial utilities asserted by Applicants are credible. Assertions of utility are credible unless "(A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is

based is inconsistent with the logic underlying the assertion." (*See*, Revised Interim Utility Guidelines Training Materials.) Further, PTO personnel are reminded that they must treat as true a statement of fact made by Applicants in relation to an asserted utility, unless countervailing evidence can be provided that shows that one of ordinary skill in the art would have a legitimate basis to doubt the credibility of such a statement. All the utilities described for the polypeptide are based on sound logic. Furthermore, the utilities for the claimed polypeptides and are ***not*** inconsistent with the logic underlying the assertion that the polypeptides are useful. Polypeptides are useful to generate antibodies, identify ligands or protein partners, evaluate expression patterns, evaluate protein activity, etc. The Office provides no evidence that the logic is seriously flawed or that the facts upon which these assertions are based are inconsistent with the logic underlying the assertions.

Furthermore, GPCR proteins have a well-established utility. Many medically significant biological processes are mediated by signal transduction pathways involving G-proteins and other second messengers, and G protein coupled seven transmembrane receptor proteins are recognized as important therapeutic targets for a wide range of diseases. According to a recently issued United States patent, nearly 350 therapeutic agents targeting GPCRs have been successfully introduced onto the market in only the last fifteen years. (*See* U.S. Patent No. 6,114,127, at col. 2, lines 45-50.) A recent journal review reported that most GPCR ligands are small and can be mimicked or blocked with synthetic analogues. That, together with the knowledge that numerous GPCRs are targets of important drugs in use today, make identification of GPCRs "a task of prime importance." (*See*, Marchese et al., Trends Pharmacol. Sci., 20(9): 370-5, 1999, copy attached hereto). Thus, the allegations that there is no well established utility for proteins of the class that the Applicants are now claiming is directly refuted by industry evidence.

In this respect, the G protein coupled receptor family is analogous to the chemical genus that was the subject of *In re Folkers*, 145 USPQ 390 (CCPA 1965) (Compound that belongs to class of compounds, members of which are recognized as useful, is considered useful under §101.) The Patent Office does not serve the public by attempting

to substitute a formulaic analysis of § 101 for the established judgment of the biopharmaceutical industry as to what is "useful." If the Patent Office is aware of any well-grounded scientific literature suggesting that GPCR's are not useful, Applicants request that it be made of record.

Art-Recognized Utility

The Utility requirement may also be satisfied by an "Art Established Utility" which means that "a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention... and the utility is specific, substantial and credible." (M.P.E.P. §2107).

Applicants note for the record that the patent office apparently agrees with Applicants' reasoning that GPCRs are useful in that the Office has granted and apparently continues to grant patents to G-protein coupled receptors, their encoding polynucleotides and antibodies directed to them ***in which no natural substrate or specific biological significance*** is ascribed to the protein. Specifically, Applicants would like to bring the following US Patents to the Office's attention:

6,518,414 Maclennan "Molecular Cloning and Expression of G-Protein Coupled Receptors" (Claims an isolated polynucleotide)
6,511,826 Li et al. "Polynucleotides Encoding Human G-Protein Chemokine Receptor (CCR5) HDGNR10" (Claims an isolated polynucleotide encoding a protein identified as a "chemokine receptor" with no specific chemokine identified)
6,372,891 Soppet et al. "Human G-Protein Receptor HPRAJ70" (Claims an antibody directed to a G-protein coupled receptor)
6,361,967 Agarwal et al. "AXOR10, A G-Protein Coupled Receptor" (Claims an isolated polynucleotide)
6,348,574 Godiska et al. "Seven Transmembrane Receptors" (Claims an antibody directed to a G-protein coupled receptor)
6,114,139 Hinuma et al. "G-Protein Coupled Receptor Protein and A DNA Encoding the Receptor" (Claims an isolated polynucleotide).
6,111,076 Fukusumi et al. "Human G-Protein Coupled Receptor (HIBCD07)" (Claims isolated polypeptide)
6,107,475 Godiska et al. "Seven Transmembrane Receptors" (Claims isolated polynucleotide and methods)
6,096,868 Halsey et al. "ECR 673: A 7-Transmembrane G-Protein Coupled Receptor" (Claims isolated polypeptide)

6,090,575 Li et al. "Polynucleotides Encoding Human G-Protein Coupled Receptor GPR1" (Claims isolated polynucleotide)
6,071,722 Elshourbagy et al. "Nucleic Acids Encoding A G-Protein Coupled 7TM Receptor (AXOR-1)" (Claims an isolated polynucleotide)
6,071,719 Halsey et al. "DNA Encoding ECR 673: A 7-Transmembrane G-Protein Coupled Receptor" (Claims an isolated polynucleotide)
6,060,272 Li et al. "Human G-Protein Coupled Receptors" (Claims isolated polynucleotide)
6,048,711 Hinuma et al. "Human G-Protein Coupled Receptor Polynucleotides" (Claims isolated polynucleotide)
6,030,804 Soppet et al. "Polynucleotides Encoding G-Protein Parathyroid Hormone Receptor HLTDG74 Polypeptides" (Claims isolated polynucleotide)
6,025,154 Li et al. "Polynucleotides Encoding Human G-Protein Chemokine Receptor HDGNR10" (Claims an isolated polynucleotide encoding a protein identified as a "chemokine receptor" with no specific chemokine identified)
5,998,164 Li et al. "Polynucleotides Encoding Human G-Protein Coupled Receptor GPRZ" (Claims isolated polynucleotide)
5,994,097 Lal et al. "Polynucleotide Encoding Human G-Protein Coupled Receptor" (Claims isolated polynucleotide)
5,958,729 Soppet et al. "Human G-Protein Receptor HCEGH45" (Claims isolated polypeptide)
5,955,309 Ellis et al. "Polynucleotide Encoding G-Protein Coupled Receptor (H7TBA62)" (Claims isolated polynucleotide)
5,948,890 Soppet et al. "Human G-Protein Receptor HPRAJ70" (Claims isolated polypeptide)
5,945,307 Glucksmann et al. "Isolated Nucleic Acid Molecules Encoding A G-Protein Coupled Receptor Showing Homology to The 5HT Family of Receptors" (Claims isolated polynucleotide)
5,942,414 Li et al. Polynucleotides Encoding Human G-Protein Coupled Receptor HIBEF51" (Claims isolated polynucleotide)
5,912,335 Bergsma et al. "G-Protein Coupled Receptor HUVCT36" (Claims isolated polynucleotide)
5,874,245 Fukusumi et al. "Human G-Protein Coupled Receptors (HIBCD07)" (Claims isolated polynucleotide)
5,871,967 Shabon et al. "Cloning of A Novel G-Protein Coupled 7TM Receptor" (Claims isolated polynucleotide)
5,869,632 Soppet et al. "Human G-Protein Receptor HCEGH45" (Claims isolated polynucleotide)
5,856,443 MacLennan et al. "Molecular Cloning and Expression of G-Protein Coupled Receptors" (Claims isolated polynucleotide)
5,834,587 Chan et al. "G-Protein Coupled Receptor, HLTEX11" (Claims isolated polypeptide)
5,776,729 Soppet et al. "Human G-Protein Receptor HGBER32" (Claims isolated polynucleotide)

5,763,218 Fujii et al. "Nucleic Acid Encoding Novel Human G-Protein Coupled Receptors" (Claims isolated polynucleotide)
5,756, 309 Soppet et al. "Nucleic Acid Encoding A Human G-Protein Receptor HPRAJ70 and Method of Producing the Receptor" (Claims isolated polynucleotide)
5,585,476 MacLennan "Molecular Cloning and Expression of G-Protein Coupled Receptors" (Claims isolated polynucleotide)
5,759,804 Godiska et al. "Isolated Nucleic Acid Encoding Seven Transmembrane Receptors" (Claims isolated polynucleotide and methods)

Applicants respectfully submit that these issued US Patents are evidence of an art recognized utility for G-protein coupled receptors whose natural ligand is unknown. If the Patent Office's position is that issued patents are ***not*** sufficient evidence of art recognition then Applicants respectfully request that this position be made of record. In the alternative, if the Patent Office wishes to take the position that these issued patents are directed to non-statutory subject matter, then Applicants respectfully request that this position also be made of record.

In view of the foregoing, Applicants respectfully requests that the rejection under 35 U.S.C. § 101 be withdrawn.

Rejections under 35 U.S.C. § 112

Claims 31, 34, and 35 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to adequately teach how to use the instant invention for the reasons that the Office gave with regard to the rejection of these claims under 35 U.S.C. § 101. Applicants respectfully disagree.

As a preliminary matter Applicants note that the rejection under 35 U.S.C. § 112, first paragraph, is incomplete and fails to set forth the specific reasons for rejection. As the M.P.E.P states, "Where a major technical rejection is proper, it should be stated with a ***full development of reasons*** rather than by a mere conclusion coupled with some stereotyped expression. (M.P.E.P § 707.07(g), emphasis added.) It appears that the Office has failed to present a "full development of reasons" with respect to the rejection of claims 31, 34, and 35 under 35 U.S.C. § 112, first paragraph.

Applicants assume, however, that the allegation that the claims were rejected under 35 U.S.C. § 112, first paragraph because the Office alleges that there is no specific,

substantial, and credible utility. However, as discussed above claims 31, 34, and 35 have a substantial, specific, and credible utility. Thus, claims 31, 34, and 35 are enabled.

In view of the foregoing, Applicants respectfully request that the rejection of claim 31, 34, and 35 under 35 U.S.C. § 112, first paragraph, be withdrawn.

Rejection under 35 U.S.C. § 102(e)

Claims 31, 34, and 35 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Gan *et al.* (U.S. Patent Publication 2002/0100067 A1). According to the Office, Applicants were not granted the benefit of the filing date of an earlier filed application under 35 U.S.C. § 119(e) because the application allegedly does not meet the requirements under 35 U.S.C. § 112, first paragraph. Applicants respectfully disagree.

As a preliminary matter Applicants respectfully submit that the Office has failed to fully develop the rejection under 35 U.S.C. § 102(e). Specifically, the Office has failed to provide the reasons for not granting the benefit under 35 U.S.C. § 119(e) of the priority document. As discussed above a major technical rejection, such as the present rejection, should have "a full development of reasons rather than [] a mere conclusion." (M.P.E.P § 707.07(g). The Office has failed to provide a fully developed reason as to why the provisional application does not comply with the requirement under 35 U.S.C. § 112, first paragraph, other than the cursory statement "for the reasons given above." Applicants respectfully request that if the rejection is maintained that a "full development of reasons" be provided so that Applicants are able to address the Office's concerns.

The priority document for the present application is a provisional application (U.S. Ser. No. 60/198,600). According to the M.P.E.P., "The filing date of a provisional application is the date on which (1) a specification which complies with 35 U.S.C. 112, first paragraph, and (2) any drawing required by 37 C.F.R. 1.81(a) are filed." (M.P.E.P § 201.04(b)). (U.S. Ser. No. 60/198,600) complied with these requirements when filed and contains a written description of the invention, how to make and use the invention, and the best mode by which to use the invention. There is nothing in the M.P.E.P, the Federal Laws, or the C.F.R. that suggests or recites that a utility requirement be satisfied in the

provisional application. Notwithstanding the foregoing, Applicants note that for at least the reasons discussed above in respect to the present application, the priority document also complies with the requirements under 35 U.S.C. § 101.

The specification of the provisional application recites how to make the polypeptide and how to use the polypeptide in the development of antibodies. The antibodies can be used to analyze protein expression in cells, tissues, or other samples that contain proteins, such as a cell lysate. The priority document also discloses how to identify binding partners for the polypeptide. Furthermore, the priority application provides a written description of the polypeptide. Therefore, the earlier filed application complies with the requirements of 35 U.S.C. § 112, first paragraph.

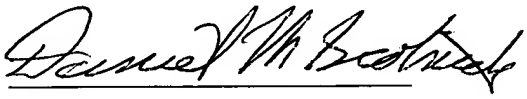
Accordingly, the Gan reference is not available as a reference under 35 U.S.C. § 102(e) since its publication date is after the filing date of the present application. In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 102(e) be withdrawn.

Conclusion

Applicants believe the claims are in condition for allowance. An early Notice of Allowance is therefore earnestly solicited. Applicants invite the Examiner to contact the undersigned at (215) 665-6928 to clarify any unresolved issues raised by this response.

Respectfully submitted,

DATE:June 25, 2003



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